

Weekly Iron and Folic Acid Supplementation As a Tool to Reduce Anemia among Primary School Children in Cambodia

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The prevalence of anemia decreased from 62% to 12% and from 57% to 26% in children 5 to 11 years of age in two rural primary schools in Kampot Province, Cambodia, after oral weekly supplementation with iron-folic acid tablets for 20 weeks and with vitamin A and mebendazole twice per year. In 12- to 15-year-old children, success was less marked. The prevalence of hookworm infestation did not change, but the number of eggs in the stool decreased drastically. The intervention had no significant influence on stunting and wasting. An integrated community approach including mass deworming, health education, and multi-micronutrient supplementation was very effective in reducing anemia in Cambodian schoolchildren and should be adopted on a larger scale.

Key words: anemia, hemoglobin concentration, stunting, wasting, age determination, parasites

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INTRODUCTION

The quality of the diet in Cambodia is poor. It starts with inappropriate breastfeeding and then is hampered by food taboos. Weaning food frequently consists of white rice soup without meat, vegetables, or fruit. The majority of people in rural areas, including many young children, eat only twice per day, mainly plain rice with small amounts of fish. Vegetables and fruits are often

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absent in the diet. Using a cutoff point of 110 g hemoglobin (Hb)/L, the UNICEF baseline survey of Community Action for Social Development in Cambodia in 1998 showed that 81% of 1348 children 6 to 59 months of age were anemic, with a mean Hb concentration of 96 g/L. In a follow-up survey in May 2000, 74% of 1588 children under 5 years of age were anemic. The prevalence is even higher for children under 2 years of age. Deficiencies of vitamins A, B, and iodine, and infections with intestinal parasites are frequent. In the first National Micronutrient Survey of Cambodia in 2000, children in 7 out of 10 survey provinces showed a prevalence of night blindness of over 1%. The National Goiter Survey in 1996–1997 revealed a goiter rate of over 12% in children ages 8 to 14. The prevalence of malnutrition is high and is the main factor undermining healthy growth and intellectual development of children in Cambodia.

In 1996, the Integrated Food Security Program was started to coordinate the efforts of national and international agencies as well as non-governmental organizations (NGOs) on the improvement of the nutritional situation in Cambodia. As part of this program, the German Technical Cooperation (GTZ) started community health activities in Kampot Province. The activity included a growth-monitoring program for children under 5 years of age, which was soon expanded with many older children in poor health condition. To take care of these older children, the Integrated Food Security Program started a school health program in 1999 in nine schools in rural areas, which was later extended to 25 schools in Kampot Province. The program included medical examination of the eyes, ears, mouth, hands, feet, and skin, as well as six monthly administrations of vitamin A (200,000 IU) and mebendazole (500 mg). Health education was also part of the program, as poor hygiene was the main cause for scabies and other skin diseases.

The only data on prevalence of anemia in Cambodia available in 1999 concerned children under 5 and adults over 15 years of age. Therefore, a school health survey was performed to collect data for the age group 5 to 14

years. The prevalence of anemia was 64% during baseline Hb determinations in this age group, so iron-folic acid tablets were given in school once a week over a period of 20 weeks to all children in first grade between the end of 1999 and June 2000. Hb concentration, anthropometric measures, and stool samples were re-examined after this intervention.

METHODS

The baseline school survey was performed in July 1999 before the end of the school term, and was repeated after the intervention in July 2000. Age, sex, weight, height, Hb concentration, and stool parasites were analyzed before and after the intervention.

Description of Study Population

Two cluster schools were selected for the study: the Wat Ang Chork primary school in Trapiang Reang (Chum Kiri District) with 1083 pupils, and the Dang Tung primary school in Dang Tung district with 609 pupils. Early dropout from school is a common problem in Cambodia. Therefore, in order to keep attrition rates low, only grade-one pupils were included in the survey. All grade-one pupils present on the day of the baseline survey were included. None of these children showed clinical signs of chronic diseases at medical examination. Moreover, micronutrient supplements that could possibly interfere with this intervention were not available in the Kampot area. For these two reasons, no particular exclusion criteria were applied.

Age Assessment

To relate Hb concentrations to age and for the assessment of stunting using height for age, correct ages are essential. This is a problem in rural Cambodian schoolchildren. In 1999, "school registration age" was not accurate and family records were not available. However, parents knew their children's "traditional zodiac date of birth." The accurate age of the children, therefore, was assessed by home visiting surveys. A special questionnaire was used, which included traditional lunar Khmer calendars for months and Chinese calendar animals for years. These data were cross-matched with questions regarding main events in the year to confirm the results.

Anthropometry

Weight was measured to the nearest 100 g using a floor scale distributed by UNICEF (Seca Corp., Hanover, MD), and height was determined to the nearest 0.1 cm by

use of a locally made tool. The indicators weight-for-height and height-for-age, respectively, were used to define "wasting" (acute malnutrition) and "stunting" (chronic malnutrition). The indicator weight-for-age was used to define "underweight" (general undernutrition). All pupils below a cutoff point of minus two standard deviations compared with an international reference population were considered malnourished. Data analysis software (Epi Info, CDC, Atlanta, GA) provided the percentage of malnourished children, based on Z-scores, referring to the standard deviation of the frequency distribution of this reference population.

Stool Analysis

Before July 1999, no mass deworming was done in the school population under investigation. During the July 1999 baseline survey, 162 stools were collected in Dang Tung School only and analyzed immediately according to Kato-Katz¹ to assess the intensity of the infestation, and according to the sodium acetate-acetic acid-formalin (SAF) method developed by Ritchie² to assess the prevalence of all intestinal parasites including protozoa. The Baermann method³ was used to assess the prevalence of *Strongyloides stercoralis*. In July 2000, 146 stools were collected and the same examinations were repeated after two deworming sessions. In addition, pupils answered a questionnaire regarding living conditions, water supply, and behavior during defecation. Stools from other schools were not analyzed in this pilot project.

Hemoglobin Assessment

The Hb concentration was estimated using the hemoglobinometer undiluted method (Lovibond, Tintometer, Salisbury, UK), which does not require a reliable electric power supply.⁴ Capillary blood was obtained by pricking a finger with a sterile lancet. The blood ran directly into the observation cell of the hemoglobinometer, where the color was compared with a series of colored glasses. Double, even triple readings were taken for all cases, with borderline results. Results obtained by this method correlated surprisingly well with corresponding certified cyanmethemoglobin determinations in an earlier study,⁴ though no value for the correlation coefficient was given. Specificity was between 66% and 99%, sensitivity between 70% and 94%, and the predictive value was between 82% and 98% when systematically compared in populations from different parts of the world.⁴ The Hb cutoff to define anemia was according to WHO guidelines⁵: under 115 g/L for children ages 5 to 11 years and under 120 g/L for children 12 to 14 years of age. Based on the correlation between the undiluted

hemoglobinometer method and the cyanmethemoglobin method,⁴ these cutoff values correspond to a range of 105 to 132 g/L and 110 to 137 g/L, respectively (confidence interval: 95%). Though this comparison shows sufficient reliability on which to base Hb estimates, certified methods for Hb determinations should be used in future studies if electricity is reliably available.

Intervention

Starting in June 1999, vitamin A (200,000 IU) and mebendazole (500 mg) were distributed every 6 months in nine schools. Vitamin B complex (1 mg each of B₁, B₂, and B₆ in two tablets/day) was provided only to those children who showed angular gingivitis as a clinical sign of vitamin B₂ deficiency. From December 1999, all children in nine schools, including the 451 pupils from this survey, received a UNICEF iron-folic acid tablet once a week (60 mg of Fe as ferrous sulfate and 0.25 mg folic acid). Teachers distributed the tablet and supervised its consumption during the teaching period of 20 weeks. No iron or folic acid was distributed during school holidays, so supplementation stopped in June 2000. The follow-up survey was done in early July 2000.

Compliance

At the end of the intervention period in 2000, tablets of vitamin A and mebendazole were shown to each subject. The pupils were asked how many of each they had taken during the past 12 months to estimate compliance with the vitamin A/mebendazole program; the same process was used for the iron-folic acid tablets. Teachers supervised intake of iron-folic acid tablets for those children who were at school but did not record the number of children absent.

Pharmaceutical Supply

All supplements came from the Central Medical Store of the Ministry of Health. The National Mother and Child Health Department provided iron-folic acid tablets and vitamin A (200,000 IU/capsule). The parasitology department of the "Centre National de Malaria" provided mebendazole (500 mg/tablet). Vitamin B complex tablets were imported from the Netherlands.

Data Analysis

The software programs EPI Info 6™ and EpiNut Anthropometry for Nutrition (CDC, Atlanta, GA) were used to analyze weight and height in terms of respective indicators for stunting (height-for-age), wasting (weight-for-height), and general undernutrition (weight-for-age).

Data are given as means \pm SD. Means of two corresponding groups were compared by use of Student's unpaired *t*-test to assess the statistical significance of differences.

RESULTS

Included in the study of grade-one pupils were 234 children in Trapiang Reang (121 male and 113 female) and 217 in Dang Tung (113 male and 104 female). The same set of parameters assessed at baseline was reassessed in the same group of children 12 months later after weekly oral iron-folic acid administration during the 20-week trial period ending with the end of term. In Trapiang Reang, 215 out of 234 pupils completed the study, as did 197 out of 217 in Dang Tung. The attrition rate was as low as 9%. In 1999, according to the pupil's age assessed prior to the study, 15% of the pupils were 12 to 15 years old, while 1 year later 31% of the pupils were in this age range. This is a very high percentage of comparably old children in grade one, and is the consequence of frequent class repetition and late entry into primary school. In Dang Tung, more than half of the children repeat grade one instead of passing on to grade two.

Age Assessment

Two-hundred-twenty-eight children had their age assessed in Trapiang Reang, and 184 in Dang Tung. A large discrepancy was found between "school registration age" and the age identified by our survey questionnaire (real age). In Trapiang Reang, the mean school-registered age was 2 years below the real age. In Dang Tung, the difference between the two means was 1 year. Only 7 out of 440 children started school at the recommended age of 6 years, while a few older pupils aged 12 to 15 were still repeating grade one.

Anthropometry

At baseline, height, weight, and age were assessed, and related indicators of malnutrition were determined in 207 children in Dang Tung and in 233 children in Trapiang Reang. Detailed results of the survey can be seen in Tables 1 and 2. Little change occurred in the prevalence of malnutrition between 1999 and 2000.

Stool Analysis

In 1999, 162 fresh stool specimens were analyzed out of a total of 217 subjects in Dang Tung. In this study, 62% out of 162 specimens were parasite positive: 42% of the stools contained hookworm, 12% *S. stercoralis*, 7%

Table 1. Anthropometric Data in Grade-One Children in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999

	Trapiang Reang			Dang Tung				
	<i>N</i>	Mean Age*	Mean Weight	Mean Height	<i>N</i>	Mean Age	Mean Weight	Mean Height
		<i>yrs</i>	<i>kg</i>	<i>cm</i>		<i>yrs</i>	<i>kg</i>	<i>cm</i>
All ages	234	9.4 (6–15)†	19.4 (12.4–32.6)	117.6 (100–140)	217	10 (6–15)	21.7 (14.2–35.4)	122.7 (99–144.3)
6–11 years	211	9.0 (6–11)	19.4 (12.4–32.6)	117.6 (100–140)	171	9.4 (6–11)	21.0 (14.2–35.4)	121.0 (99–144.3)
12–15 years	23	12.7 (12–15)	23.9 (16.1–32.6)	127.9 (116–140)	46	12.5 (12–15)	24.4 (17.6–32.7)	129.1 (113–142)

*Mean age is the calculated “real age,” as opposed to mainly biased “school registered age.”

†Numbers in parentheses are ranges.

Trichuris trichiura, 6.5% *Entamoeba histolitica*, 4% *Enterobius*, 2.5% *Hymenolepis nana*, 2% *Ascaris lumbricoides*, and 1% *Giardia*. Stools with mixed infection were common. In 2000, parasite infestation was still a prevalent problem: 49% of stool specimens were parasite positive compared with 62% in 1999. Although 40% of stools remained hookworm infected, the infestation intensity decreased considerably. Infestation of over 1000 eggs/g decreased from 2% to zero, infestation of 100 to 1000 eggs/g decreased from 20% to 9%, and infestation of 100 eggs/g increased from 20% to 30% in all specimens under inspection.

Hemoglobin Assessment

Two-hundred-thirty-four blood samples were collected in Trapiang Reang, 217 in Dang Tung. About two-thirds of pupils in both schools were anemic in 1999 (Table 3). Anemia was more prevalent in both sites in 12- to 14-year-old children compared with younger age groups. No significant difference was seen between sexes. All cases of “severe” anemia in Trapiang Reang (Hb < 97 g/L) seen in 1999 had disappeared after the intervention. The distribution of Hb concentration

showed a marked shift towards higher values between 1999 and 2000 in Trapiang Reang (Figure 1).

Compliance

Based on recall by children, the mean number of iron-folic acid tablets taken in Trapiang Reang was 18 out of 20; this number was 14 out of 20 in Dang Tung. These figures signal good or satisfactory compliance, respectively. However, the estimate is based on a comparably small random sample, which permits no valid statistical evaluation.

DISCUSSION

This study took advantage of an opportunity to obtain important information before and after intervention with supplements and drugs that reduce the risk of anemia caused by inadequate iron intake, parasitic infections, and vitamin A deficiency. These data provide useful information as a basis for future work among schoolchildren in Cambodia. Moreover, the prevalence of incorrect age data was estimated, which is important

Table 2. Prevalence of Acute (Wasting) and Chronic (Stunting) Malnutrition and Undernutrition in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999 and July 2000 Before and After Weekly Iron-Folic Acid Supplementation*

Place and Year	<i>N</i>	Acute Malnutrition (Weight-for-Height)	Chronic Malnutrition (Height-for-Age)	General Undernutrition (Weight-for-Age)
			<i>% pupils < -2 SD</i>	
Trapiang Reang School 1999	233	9%	60%	59%
Trapiang Reang School 2000	215	10%	55%	53%
Dang Tung School 1999	207	4%	45%	42%
Dang Tung School 2000	197	4%	43%	38%

*No significant improvement of anthropometric data was observed after the intervention.

Table 3. Prevalence of Anemia among Grade-One Pupils in Two Rural Primary Schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools) in July 1999 and July 2000 Before and After Weekly Iron-Folic Acid Supplementation

	Trapiang Reang			Dang Tung		
Before Intervention (1999)						
Age group	5–11 yrs (N = 211)	12–14 yrs (N = 23)*	All (N = 234)	5–11 yrs (N = 171)	12–14 yrs (N = 46)	All (N = 217)
Anemia†	130 (62%)	19 (83%)	149 (64%)	98 (57%)	42 (91%)	140 (65%)
After Intervention (2000)						
Age group	5–11 yrs (N = 160)	12–14 yrs (N = 52)	All (N = 212)	5–11 yrs (N = 122)	12–14 yrs (N = 70)	All (N = 192)
Anemia	19 (12%)	23 (44%)	42 (20%)	32 (26%)	38 (55%)	70 (37%)

*The sample size in group 12–14 years of age increased in 2000 as children 5–11 years of age in 1999 became 1 year older.

†Anemia was defined as hemoglobin <115 g/L for age group 5–11 years; <120 g/L for age group 12–14 years. Anemia was significantly more prevalent in the older age group at both locations (Student's *t*-test; $P < 0.0001$). No significant differences were seen between sexes (data not shown).

for the assessment of stunting, wasting, and overall nutritional status.

Correct assessment of the age is a prerequisite for valid comparison of growth measurements to a corresponding reference population. As most official birth registers were lost during the war in Cambodia, parents registered their children at school when they perceived they had reached an appropriate height. Since the majority of children are small for their age, their parents tend to send them to school late. Obtaining correct age data involved interviewing parents and caretakers during home visits to determine the correct birth date. Our data showed that the school registration age in rural Cambodia could not be used for comparative studies of anthro-

pometric measurements based on age. Proper data on age for school registration need to be derived.

Prevalence of Stunting and Wasting

Roughly half of the children 5 to 11 years of age, and close to 90% of those 12 years and over were stunted. Supplementation with iron, folic acid, vitamin A, and vitamin B complex for those with clinical vitamin B deficiency symptoms did not significantly improve the situation. This finding suggests that protein, calories, and perhaps other micronutrients that were not supplemented were still in short supply. Moreover, improvement of growth in height after nutrition intervention was mostly seen in younger children and infants, not in school-age children. Accurate data on food intake were not available, so we could not analyze differences in this parameter between the two locations. Clinical symptoms such as anemic pallor were frequent, and angular gingivitis was seen in 10% to 15% of pupils in both schools during the health surveys.

Experience and Compliance with Iron-Folic Acid Intervention

This is the first Hb survey done in rural schools in Cambodia. It showed a high prevalence of anemia, which is likely to impair children's health and school performance.^{6,7} This probably contributed to the high number of children (approximately 50%) repeating grade one.

The low Hb values suggested the need to start an intervention program immediately. Thus, the interven-

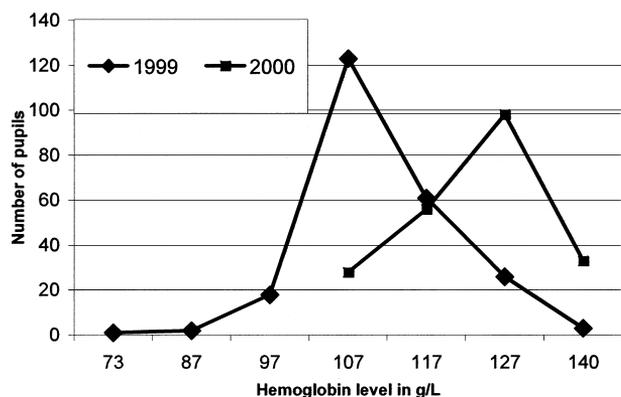


Figure 1. Distribution of hemoglobin concentrations before (1999) and after (2000) weekly iron-folic acid supplementation in grade-one children in two rural primary schools in Kampot Province, Cambodia (Trapiang Reang and Dang Tung Schools).

tion was not part of a preplanned trial, but rather a response to an urgent need. This situation, as well as ethical considerations, explains the lack of a placebo group, which would have been desirable to assess the specific impact of the intervention. However, in spite of this, a marked impact of the intervention on Hb concentration and a marked reduction in the prevalence of anemia became obvious.

The reduction in prevalence of anemia strongly supports the usefulness of iron-folic acid supplementation in schoolchildren 6 to 12 years of age. At the beginning of the intervention, some children complained about stomachache after ingestion of the iron-folic acid pills. The frequency of gastrointestinal side effects is known to relate to the iron dose,⁸ but symptoms were most common in pupils who came to school without breakfast. Interviews with pupils showed that 30% went to school on an empty stomach. Although it was recommended that students eat some food prior to weekly iron distribution, this was not possible in all cases, leading to about 5% of schoolchildren avoiding school on the day tablets were distributed. During the 20-week school period in 1999–2000, tablets were handed out 20 times. On average, schoolchildren accepted the tablets 18 times and 14 times in Trapiang Reang and Dang Tung, respectively, corresponding to a compliance of approximately 90% and 70%, respectively. Weak teacher supervision in some classrooms in Dang Tung was identified as the main cause of the lower compliance and effectiveness at this location.

A problem with the interpretation of these data is that we cannot separate the impact of iron supplementation on anemia reduction from that of the vitamin A and mebendazole interventions. As the compliance with vitamin A and mebendazole distribution was high in both schools (because of the supervised distribution by health center staff), it is likely that the lower compliance with iron intake in Dang Tung was the main cause of the lower success regarding anemia reduction in that school. Nevertheless, the regimen of one tablet of iron per week handed out at school was satisfactory.

Regarding the degree of malnutrition, no significant changes were observed before or after intervention. Both surveys were done in July at the beginning of the rainy season. Without famine or war, wasting is mainly caused by diarrhea due to unsafe water and food. As the pupils were living in the same environmental conditions during both surveys, no change was expected. The small decrease observed in the prevalence of stunting may be interpreted as an indication of slightly improved food security or as the consequence of the intervention. Further work needs to be done to improve food security to insure proper nutrition for children before and after birth.

Stool Analysis

During the baseline survey in 1999, 42% of the children were infected with hookworms and 12% with *S. stercoralis*. Both parasites enter the body from contaminated soil via the skin of feet. The reason for such high prevalence is that 84% of the homes had no latrines. As 90% of the children did not wear shoes during defecation, frequent re-infection with hookworms was likely. Indeed, the follow-up survey in 2000 found little reduction in the prevalence of hookworm infestation, although the number of hookworm eggs counted in the stool had decreased markedly. This is a success regarding the impact of hookworm infestation on anemia, as the extent of intestinal bleeding correlates with the number of hookworms in the intestine.⁹ *S. stercoralis* infestation decreased by 50%. Therefore, intervention with mebendazole is a useful tool to reduce intestinal blood losses, but needs to be given on a regular basis to cope with frequent reinfestation.

CONCLUSIONS

An integrated community approach including mass deworming, health education, and multi-micronutrient supplementation was very effective in reducing anemia in schoolchildren in Cambodia and should be adopted on a larger scale.

A number of lessons can be learned from the observations reported:

1. Growth assessment needs to be related to correct age. This is a critical issue in Cambodia, as birth registers are often missing or inaccurate, resulting in parents sending their children to school late.
2. The Cambodian diet is deficient in many ways. The results suggest that the supplementation of iron, folic acid, vitamin A, and B vitamins are not sufficient to reduce the prevalence of stunting. Additional nutrients are needed, including a sufficient supply of protein, calories, and other micronutrients.
3. Anemia in this study occurred in two-thirds of grade-one schoolchildren 5 to 11 years of age and in up to 80% to 90% of children ≥ 12 years of age. Though the database is limited, supplementation of iron and folic acid in these age groups seems urgently needed on a larger scale.
4. Weekly iron-folic acid supplementation is a useful tool to mitigate the extent and prevalence of anemia in grade-one Cambodian children. Supplementation with other micronutrients, such as vitamin A and possibly others, as well as hookworm control, are likely to be helpful in this effort. To improve compliance, however, it may be advisable to use a lower single dose of iron than the 60 mg used in this study. It may also help to provide the iron supplement

together with or shortly after school meals, since many children come to school without breakfast.

5. Regular mebendazole administration proved useful in reducing the number of hookworm eggs in the intestine. To improve the hygienic situation and to reduce hookworm infestation, latrine programs and education on how to maintain them are needed. In addition, children should wear shoes to reduce infestation with hookworms.

Based on results from the pilot weekly iron supplementation program reported herein, the program has been expanded to 25 Cambodian schools supported by GTZ's Rural Development Program. Fifteen thousand primary school children receive weekly supplementation, many of them since late 1999. The results of this survey suggest that such an intervention is very cost-effective, since iron-folic acid tablets cost around 5 cents US per child per year.

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